



Psoriasis: assessment and management

Clinical guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should <u>assess and reduce the environmental impact of implementing NICE recommendations</u> wherever possible.

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This guideline is the basis of QS40.

Overview

This guideline covers assessing and managing psoriasis in adults, young people and children. It aims to improve long-term disease control and quality of life for people with psoriasis.

Who is it for?

- Healthcare professionals
- Commissioners and providers
- Children and adults with a diagnosis of psoriasis, and their families and carers

Introduction

Psoriasis is an inflammatory skin disease that typically follows a relapsing and remitting course. The prevalence of psoriasis is estimated to be around $1.3-2.2\%^{[1]}$ in the UK. Psoriasis can occur at any age, although is uncommon in children (0.71%) and the majority of cases occur before 35 years. Psoriasis is associated with joint disease in a significant proportion of patients (reported in one study at 13.8%)^[2].

Plaque psoriasis is characterised by well-delineated red, scaly plaques that vary in extent from a few patches to generalised involvement. It is by far the most common form of the condition (about 90% of people with psoriasis). Other types of psoriasis include guttate psoriasis and pustular (localised or generalised) forms. Distinctive nail changes occur in around 50% of all those affected and are more common in people with psoriatic arthritis.

Healthcare professionals and patients using the term psoriasis are usually referring to plaque psoriasis, and unless stipulated otherwise, 'psoriasis' is used in this way in the guideline. The phrase 'difficult-to-treat sites' encompasses the face, flexures, genitalia, scalp, palms and soles and are so-called because psoriasis at these sites may have especially high impact, may result in functional impairment, requires particular care when prescribing topical therapy and can be resistant to treatment.

Psoriasis for many people results in profound functional, psychological, and social morbidity, with consequent reduced levels of employment and income. Factors that contribute to this include symptoms related to the skin (for example, chronic itch, bleeding, scaling and nail involvement), problems related to treatments, psoriatic arthritis, and the effect of living with a highly visible, stigmatising skin disease. Even people with minimal involvement state that psoriasis has a major effect on their life. Several studies have also reported that people with psoriasis, particularly those with severe disease, may be at increased risk of cardiovascular disease, lymphoma and non-melanoma skin cancer.

A wide variety of treatment options are available. Some are expensive and some are accessed only in specialist care; all require monitoring. The treatment pathway in this guideline begins with active topical therapies. The Guideline Development Group (GDG) acknowledged that the use of emollients in psoriasis was already widespread and hence the evidence review was limited to active topical therapies for psoriasis.

In this guideline, first-line therapy describes traditional topical therapies (such as corticosteroids, vitamin D and vitamin D analogues, dithranol and tar preparations). Second-line therapy includes

the phototherapies (broad- or narrow-band ultraviolet B light and psoralen plus UVA light [PUVA]) and systemic non-biological agents such as ciclosporin, methotrexate and acitretin. Third-line therapy refers to systemic biological therapies such as the tumour necrosis factor antagonists adalimumab, etanercept and infliximab, and the monoclonal antibody ustekinumab that targets interleukin-12 (IL-12) and IL-23. NICE has published technology appraisals on the use of biological drugs, and this guideline incorporates recommendations from these appraisals where relevant (listed in alphabetical order). Biologic treatment is complicated by a poor response in a minority of people, and this guideline reviewed the literature for the use of a second biological drug.

For most people, psoriasis is managed in primary care, with specialist referral being needed at some point for up to 60% of people. Supra-specialist (level 4)^[4] tertiary care is required in the very small minority with especially complex, treatment resistant and/or rare manifestations of psoriasis.

A recent UK audit in the adult population demonstrated wide variations in practice, and in particular, access to specialist treatments (including biological therapy), appropriate drug monitoring, specialist nurse support and psychological services^[s].

This guideline covers people of all ages and aims to provide clear recommendations on the management of all types of psoriasis. The term 'people' is used to encompass all ages. 'Children' refers to those up to 12 years, who become 'young people' thereafter, before merging with the adult population by 18 years of age. The GDG have focused on areas most likely to improve the management and delivery of care for a majority of people affected, where practice is very varied and/or where clear consensus or guidelines on treatments are lacking. It is hoped that this guideline will facilitate the delivery of high-quality healthcare and improved outcomes for people with psoriasis.

Parisi R, Griffiths CEM, Ashcroft DM (2011) Systematic review of the incidence and prevalence of psoriasis. British Journal of Dermatology 165: e5.

^[2] Ibrahim G, Waxman R, Helliwell PS (2009) The prevalence of psoriatic arthritis in people with psoriasis. Arthritis and Rheumatism 61:1373–8.

^[3] Please refer to the <u>British National Formulary and the British National Formulary for Children</u> for guidance on use of emollients.

^[4]Level 4 care is defined as usually taking place entirely within an acute hospital and is carried out by consultant dermatologists and a range of other healthcare professionals with special skills in the management of complex and/or rare skin disorders – see Quality Standards for Dermatology:

providing the right care for people with skin conditions.

^[s] Eedy DJ, Griffiths CE, Chalmers RJ et al. (2009) Care of patients with psoriasis: an audit of U.K. services in secondary care. British Journal of Dermatology. 160: 557–64.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

Assessment tools for disease severity and impact and when to refer for specialist care

- For people with any type of psoriasis assess:
 - disease severity
 - the impact of disease on physical, psychological and social wellbeing
 - whether they have psoriatic arthritis
 - the presence of comorbidities.
- Following assessment in a non-specialist setting, refer people for dermatology specialist advice if:
 - there is diagnostic uncertainty or
 - any type of psoriasis is severe or extensive, for example more than 10% of the body surface area is affected or
 - any type of psoriasis cannot be controlled with topical therapy or
 - acute guttate psoriasis requires phototherapy (see recommendation 1.4.1.1) or
 - nail disease has a major functional or cosmetic impact or
 - any type of psoriasis is having a major impact on a person's physical, psychological or social wellbeing.

Assessment and referral for psoriatic arthritis

• As soon as psoriatic arthritis is suspected, refer the person to a rheumatologist for assessment and advice about planning their care.

Identification of comorbidities

• Discuss risk factors for cardiovascular comorbidities with people who have any type of psoriasis (and their families or carers where appropriate). Where appropriate offer preventative advice, healthy lifestyle information and support for behavioural change tailored

- to meet the needs of the individual in line with the following NICE guidance:
 - Cardiovascular disease: risk assessment and reduction, including lipid modification
 - Obesity prevention
 - Type 2 diabetes prevention: population and community-level interventions
 - Cardiovascular disease prevention
 - Alcohol-use disorders: prevention
 - Stop smoking interventions and services
 - Physical activity: brief advice for adults in primary care
 - Physical activity in the workplace
 - Physical activity for children and young people.

Topical therapy: general recommendations

 Offer practical support and advice about the use and application of topical treatments. Advice should be provided by healthcare professionals who are trained and competent in the use of topical therapies. Support people to adhere to treatment in line with the NICE guideline on medicines adherence. Also see the NICE guideline on medicines optimisation.

Topical therapy: topical treatment of psoriasis affecting the trunk and limbs

• Offer a potent corticosteroid applied once daily plus vitamin D or a vitamin D analogue applied once daily (applied separately, one in the morning and the other in the evening) for up to 4 weeks as initial treatment for adults with trunk or limb psoriasis.

Phototherapy (broad- or narrow-band ultraviolet B light)

• Offer narrowband ultraviolet B (UVB) phototherapy to people with plaque or guttate-pattern psoriasis that cannot be controlled with topical treatments alone. Treatment with narrowband UVB phototherapy can be given 3 or 2 times a week depending on patient preference. Tell people receiving narrowband UVB that a response may be achieved more quickly with treatment 3 times a week.

Systemic non-biological therapy

- Offer systemic non-biological therapy to people with any type of psoriasis if:
 - it cannot be controlled with topical therapy and
 - it has a significant impact on physical, psychological or social wellbeing and
 - one or more of the following apply:
 - psoriasis is extensive (for example, more than 10% of body surface area affected or a <u>Psoriasis Area and Severity Index</u> (PASI)^[a] score of more than 10) or
 - psoriasis is localised and associated with significant functional impairment and/or high levels of distress (for example severe nail disease or involvement at highimpact sites) or
 - phototherapy has been ineffective, cannot be used or has resulted in rapid relapse (rapid relapse is defined as greater than 50% of baseline disease severity within 3 months).

Choice of drugs (systemic non-biological therapy)

• Offer methotrexate^[7] as the first choice of systemic agent for people with psoriasis who fulfil the criteria for systemic therapy (see previous recommendation 1.5.2.1) except in the circumstances described in recommendations 1.5.2.4 and 1.5.2.12.

Changing to an alternative biological drug (systemic biological therapy)

- Consider changing to an alternative biological drug in adults if:
 - the psoriasis does not respond adequately to a first biological drug as defined in NICE technology appraisals^[s] (at 10 weeks after starting treatment for infliximab, 12 weeks for etanercept, ixekizumab and secukinumab, and 16 weeks for adalimumab and ustekinumab; primary failure) **or**
 - the psoriasis initially responds adequately but subsequently loses this response, (secondary failure) or
 - the first biological drug cannot be tolerated or becomes contraindicated.

The PASI is also available from the <u>British Association of Dermatologists</u> website.

At the time of publication (October 2012), methotrexate did not have UK marketing authorisation

for this indication in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's <u>Good practice in prescribing medicines – guidance for doctors</u> for further information.

[8] NICE technology appraisal guidance <u>103</u>, <u>134</u>, <u>146</u>, <u>180</u>, <u>350</u> and <u>442</u>.

1 Recommendations

The following guidance is based on the best available evidence. The <u>full guideline</u> gives details of the methods and the evidence used to develop the guidance.

The guidance covers people of all ages with all types of psoriasis. The recommendations were developed after discussion of the relevance of the evidence to children, young people and adults with psoriasis. If recommendations are age-limited or specific to disease type, they are clearly indicated as such.

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient should provide informed consent, which should be documented. See the General Medical Council's <u>Good practice in prescribing medicines – guidance for doctors</u>. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations.

Before prescribing any intervention for use in children, healthcare professionals should refer to the specific SPC and the BNF for Children.

People have the right to be involved in discussions and make informed decisions about their care, as described in <u>your care</u>.

<u>Making decisions using NICE guidelines</u> explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

1.1 Principles of care

- 1.1.1.1 Offer people with any type of psoriasis (and their families or carers), support and information tailored to suit their individual needs and circumstances, in a range of different formats so they can confidently understand:
 - their diagnosis and treatment options

- relevant lifestyle risk factors
- when and how to treat their condition
- how to use prescribed treatments safely and effectively (for example, how to apply topical treatments, how to minimise the risk of side effects through monitoring for safety of medicines)
- when and how to seek further general or specialist review
- strategies to deal with the impact on their physical, psychological and social wellbeing.

Also see the NICE guidelines on <u>behaviour change</u>: <u>individual approaches</u> and behaviour change: general approaches.

- 1.1.1.2 When offering treatments to a person with any type of psoriasis:
 - ensure the treatment strategy is developed to meet the person's health goals so that the impact of their condition is minimised and use relevant assessment tools to ensure these goals are met
 - take into account the age and individual circumstances of the person, disease phenotype, severity and impact, co-existing psoriatic arthritis, comorbidities and previous treatment history
 - discuss the risks and benefits of treatment options with the person (and their families or carers where appropriate). Where possible use absolute risk and natural frequency [9]
 - discuss the importance of adherence to treatment for optimising outcomes.

For more information see the NICE guidelines on <u>medicines adherence</u> and <u>medicines</u> optimisation.

- 1.1.1.3 Assess whether support and information need updating or revising at every review or interaction with the person, in particular:
 - during transition from children's services to adult services
 - when new interventions become available
 - when the person's disease severity or circumstances (for example, in terms of comorbidities or lifestyle) change.

- See also the NICE guideline on <u>transition from children's to adults' services for young</u> people using health or social care services.
- 1.1.1.4 Provide a single point of contact to help people with all types of psoriasis (and their families or carers where appropriate) access appropriate information and advice about their condition and the services available at each stage of the care pathway.
- 1.1.1.5 NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in the NICE guideline on <u>patient experience in adult NHS</u> services.

1.2 Assessment and referral

1.2.1 Assessment tools for disease severity and impact and when to refer for specialist care

- 1.2.1.1 For people with any type of psoriasis assess:
 - disease severity
 - the impact of disease on physical, psychological and social wellbeing
 - whether they have psoriatic arthritis
 - the presence of comorbidities.
- 1.2.1.2 Assess the severity and impact of any type of psoriasis:
 - at first presentation
 - before referral for specialist advice and at each referral point in the treatment pathway
 - to evaluate the efficacy of interventions.
- 1.2.1.3 When assessing the disease severity in any healthcare setting, record:
 - the results of a static Physician's Global Assessment (classified as clear, nearly clear,

- mild, moderate, severe or very severe)[10]
- the patient's assessment of current disease severity, for example, using the static Patient's Global Assessment (classified as clear, nearly clear, mild, moderate, severe or very severe)
- the body surface area affected
- any involvement of nails, high-impact and difficult-to-treat sites (for example, the face, scalp, palms, soles, flexures and genitals)
- any systemic upset such as fever and malaise, which are common in unstable forms of psoriasis such as erythroderma or generalised pustular psoriasis.
- 1.2.1.4 In specialist settings, use a validated tool to assess severity of psoriasis, for example the <u>Psoriasis Area and Severity Index</u> (PASI)^[11] (in addition to the assessments indicated in recommendation 1.2.1.3).
- 1.2.1.5 Be aware that:
 - PASI and body surface area are not validated for use in children and young people
 - erythema may be underestimated in people with darker skin types, such as skin types V and VI on the Fitzpatrick scale^[12].
- 1.2.1.6 Use the Nail Psoriasis Severity Index^[13] to assess nail disease in specialist settings:
 - if there is a major functional or cosmetic impact or
 - before and after treatment is initiated specifically for nail disease.
- 1.2.1.7 Assess the impact of any type of psoriasis on physical, psychological and social wellbeing by asking:
 - what aspects of their daily living are affected by the person's psoriasis
 - how the person is coping with their skin condition and any treatments they are using
 - if they need further advice or support
 - if their psoriasis has an impact on their mood

- if their psoriasis causes them distress (be aware the patient may have levels of distress and not be clinically depressed)
- if their condition has any impact on their family or carers.

Ask children and young people age-appropriate questions.

- 1.2.1.8 In specialist settings, and if practical in non-specialist settings, use a validated tool to assess the impact of any type of psoriasis on physical, psychological and social wellbeing, for example the:
 - Dermatology Life Quality Index (DLQI)[14],[15] for adults or
 - Children's Dermatology Life Quality Index (CDLQI)[16] for children and young people.
- 1.2.1.9 When using an assessment tool for a person with any type of psoriasis:
 - take account of their age, any disabilities (such as physical, visual or cognitive impairment), and any language or other communication difficulties, and provide help and support if needed^[14]
 - ensure that the chosen assessment tool continues to be a sufficiently accurate measure.
- 1.2.1.10 Following assessment in a non-specialist setting, refer people for dermatology specialist advice if:
 - there is diagnostic uncertainty or
 - any type of psoriasis is severe or extensive, for example more than 10% of the body surface area is affected or
 - any type of psoriasis cannot be controlled with topical therapy or
 - acute guttate psoriasis requires phototherapy (see recommendation 1.4.1.1) or
 - nail disease has a major functional or cosmetic impact or
 - any type of psoriasis is having a major impact on a person's physical, psychological or social wellbeing.
- 1.2.1.11 People with generalised pustular psoriasis or erythroderma should be referred

immediately for same-day specialist assessment and treatment.

1.2.1.12 Refer children and young people with any type of psoriasis to a specialist at presentation.

1.2.2 Assessment and referral for psoriatic arthritis

- 1.2.2.1 Offer annual assessment for psoriatic arthritis to people with any type of psoriasis. Assessment is especially important within the first 10 years of onset of psoriasis.
- 1.2.2.2 Use a validated tool to assess adults for psoriatic arthritis in primary care and specialist settings, for example the Psoriasis Epidemiological Screening Tool (PEST)^[17]. Be aware that the PEST does not detect axial arthritis or inflammatory back pain.
- 1.2.2.3 As soon as psoriatic arthritis is suspected, refer the person to a rheumatologist for assessment and advice about planning their care. Also see the NICE guideline on spondyloarthritis in over 16s.

1.2.3 Identification of comorbidities

- 1.2.3.1 Offer adults with severe psoriasis^[18] of any type a cardiovascular risk assessment at presentation using a validated risk estimation tool. Offer further assessment of cardiovascular risk every 5 years, or more frequently if indicated following assessment. For further information see the NICE guideline on <u>cardiovascular</u> disease: risk assessment and reduction, including lipid modification.
- 1.2.3.2 Discuss risk factors for cardiovascular comorbidities with people who have any type of psoriasis (and their families or carers where appropriate). Where appropriate offer preventative advice, healthy lifestyle information and support for behavioural change tailored to meet the needs of the individual in line with the following NICE guidance:
 - Cardiovascular disease: risk assessment and reduction, including lipid modification
 - Obesity prevention
 - Type 2 diabetes prevention: population and community-level interventions

- Cardiovascular disease prevention
- Alcohol-use disorders: prevention
- Stop smoking interventions and services
- Physical activity: brief advice for adults in primary care
- Physical activity in the workplace
- Physical activity for children and young people
- 1.2.3.3 For people with multiple comorbidities and/or multimorbidities and any type of psoriasis needing second- or third-line therapy, ensure multidisciplinary working and communication between specialties and, if needed, interdisciplinary team working (for example when both skin and joints are significantly affected).
- 1.2.3.4 Be aware that psoriasis of any type, especially if severe^[19], is a risk factor for venous thromboembolism in adults, and:
 - explain this risk to adults with any type of psoriasis
 - offer advice on how to minimise the risk (for example, during hospital admission, surgery, or periods of immobility)
 - manage the risk in line with the NICE guideline on <u>venous thromboembolism in over</u>
 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary
 embolism.
- 1.2.3.5 Assess whether people with any type of psoriasis are depressed when assessing disease severity and impact, and when escalating therapy. If appropriate offer information, advice and support in line with the NICE guidelines on depression in adults with a chronic physical health problem and depression in children and young people.

1.3 Topical therapy

The treatment pathway in this guideline begins with active topical therapies. The GDG acknowledged that the use of emollients in psoriasis was already widespread and hence the evidence review was limited to active topical therapies for psoriasis. Please refer to the BNF and

BNF for children for guidance on use of emollients.

1.3.1 General recommendations

- 1.3.1.1 Offer people with psoriasis topical therapy as first-line treatment.
- 1.3.1.2 Offer second- or third-line treatment options (phototherapy or systemic therapy) at the same time when topical therapy alone is unlikely to adequately control psoriasis, such as:
 - extensive disease (for example more than 10% of body surface area affected) or
 - at least 'moderate' on the static Physician's Global Assessment or
 - where topical therapy is ineffective, such as nail disease.

See also recommendations 1.2.1.9; 1.4.1.1; 1.5.2.1; 1.5.3.4; 1.5.3.6; 1.5.3.8 and 1.5.3.10.

1.3.1.3 Offer practical support and advice about the use and application of topical treatments. Advice should be provided by healthcare professionals who are trained and competent in the use of topical therapies. Support people to adhere to treatment in line with the NICE guideline on medicines adherence. Also see the NICE guideline on medicines adherence. Also see

1.3.1.4 When offering topical agents:

- take into account patient preference, cosmetic acceptability, practical aspects of application and the site(s) and extent of psoriasis to be treated
- discuss the variety of formulations available and, depending on the person's preference, use:
 - cream, lotion or gel for widespread psoriasis
 - lotion, solution or gel for the scalp or hair-bearing areas
 - ointment to treat areas with thick adherent scale
- be aware that topical treatment alone may not provide satisfactory disease control, especially in people with psoriasis that is extensive (for example more than 10% of body surface area affected) or at least 'moderate' on the static Physician's Global

- Assessment.
- 1.3.1.5 If a person of any age with psoriasis requiring topical therapy has a physical disability, or cognitive or visual impairment offer advice and practical support that take into account the person's individual needs.
- 1.3.1.6 Arrange a review appointment 4 weeks after starting a new topical treatment in adults, and 2 weeks after starting a new topical treatment in children, to:
 - evaluate tolerability, toxicity, and initial response to treatment (including measures of severity and impact described in recommendations 1.2.1.3, 1.2.1.6 and 1.2.1.7)
 - reinforce the importance of adherence when appropriate
 - reinforce the importance of a 4 week break between courses of potent/very potent corticosteroids (see recommendation 1.3.1.10).

If there is little or no improvement at this review, discuss the next treatment option with the person.

- 1.3.1.7 Discuss with people whose psoriasis is responding to topical treatment (and their families or carers where appropriate):
 - the importance of continuing treatment until a satisfactory outcome is achieved (for example clear or nearly clear) or up to the recommended maximum treatment period for corticosteroids (see sections <u>1.3.2</u>, <u>1.3.3</u> and <u>1.3.4</u>)
 - that relapse occurs in most people after treatment is stopped
 - that after the initial treatment period topical treatments can be used when needed to maintain satisfactory disease control.
- 1.3.1.8 Offer people with psoriasis a supply of their topical treatment to keep at home for the self-management of their condition.
- 1.3.1.9 In people whose psoriasis has not responded satisfactorily to a topical treatment strategy, before changing to an alternative treatment:
 - discuss with the person whether they have any difficulties with application, cosmetic acceptability or tolerability and where relevant offer an alternative formulation

- consider other possible reasons for non-adherence in line with the NICE guideline on medicines adherence.
- Also see the NICE guideline on <u>medicines optimisation</u>.

How to use corticosteroids safely^[20]

- 1.3.1.10 Be aware that continuous use of potent or very potent corticosteroids may cause:
 - irreversible skin atrophy and striae
 - psoriasis to become unstable
 - systemic side effects when applied continuously to extensive psoriasis (for example more than 10% of body surface area affected).
 - Explain the risks of these side effects to people undergoing treatment (and their families or carers where appropriate) and discuss how to avoid them.
- 1.3.1.11 Aim for a break of 4 weeks between courses of treatment with potent or very potent corticosteroids. Consider topical treatments that are not steroid-based (such as vitamin D or vitamin D analogues or coal tar) as needed to maintain psoriasis disease control during this period.
- 1.3.1.12 When offering a corticosteroid for topical treatment select the potency and formulation based on the person's need.
- 1.3.1.13 Do not use very potent corticosteroids continuously at any site for longer than 4 weeks.
- 1.3.1.14 Do not use potent corticosteroids continuously at any site for longer than 8 weeks.
- 1.3.1.15 Do not use very potent corticosteroids in children and young people.
- 1.3.1.16 Offer a review at least annually to adults with psoriasis who are using intermittent or short-term courses^[21] of a potent or very potent corticosteroid (either as monotherapy or in combined preparations) to assess for the presence of steroid atrophy and other adverse effects.

1.3.1.17 Offer a review at least annually to children and young people with psoriasis who are using corticosteroids of any potency (either as monotherapy or in combined preparations) to assess for the presence of steroid atrophy and other adverse effects.

1.3.2 Topical treatment of psoriasis affecting the trunk and limbs

- 1.3.2.1 Offer a potent corticosteroid applied once daily plus vitamin D or a vitamin D analogue applied once daily (applied separately, one in the morning and the other in the evening) for up to 4 weeks as initial treatment for adults with trunk or limb psoriasis.
- 1.3.2.2 If once-daily application of a potent corticosteroid plus once-daily application of vitamin D or a vitamin D analogue does not result in clearance, near clearance or satisfactory control of trunk or limb psoriasis in adults after a maximum of 8 weeks^[22], offer vitamin D or a vitamin D analogue alone applied twice daily.
- 1.3.2.3 If twice-daily application of vitamin D or a vitamin D analogue does not result in clearance, near clearance or satisfactory control of trunk or limb psoriasis in adults after 8–12 weeks, offer either:
 - a potent corticosteroid applied twice daily for up to 4 weeks or
 - a coal tar preparation applied once or twice daily. [22]
- 1.3.2.4 If a twice-daily potent corticosteroid or coal tar preparation cannot be used or a once-daily preparation would improve adherence in adults offer a combined product containing calcipotriol monohydrate and betamethasone dipropionate applied once daily for up to 4 weeks.
- 1.3.2.5 Offer treatment with very potent corticosteroids in adults with trunk or limb psoriasis only:
 - in specialist settings under careful supervision
 - when other topical treatment strategies have failed
 - for a maximum period of 4 weeks.
- 1.3.2.6 Consider short-contact dithranol for treatment-resistant psoriasis of the trunk

or limbs and either:

- give educational support for self-use or
- ensure treatment is given in a specialist setting.
- 1.3.2.7 For children and young people with trunk or limb psoriasis consider^[23] either:
 - calcipotriol applied once daily (only for those over 6 years of age) or
 - a potent corticosteroid applied once daily (only for those over 1 year of age).
- 1.3.3 Topical treatment of psoriasis affecting the scalp
- 1.3.3.1 Offer a potent corticosteroid^[24] applied once daily for up to 4 weeks^[25] as initial treatment for people with scalp psoriasis.
- 1.3.3.2 Show people with scalp psoriasis (and their families or carers where appropriate) how to safely apply corticosteroid topical treatment.
- 1.3.3.3 If treatment with a potent corticosteroid^[24] does not result in clearance, near clearance or satisfactory control of scalp psoriasis after 4 weeks^[25] consider:
 - a different formulation of the potent corticosteroid (for example, a shampoo or mousse) and/or
 - topical agents to remove adherent scale (for example, agents containing salicylic acid, emollients and oils) before application of the potent corticosteroid.
- 1.3.3.4 If the response to treatment with a potent corticosteroid [24] for scalp psoriasis remains unsatisfactory after a further 4 weeks [22], [43] of treatment offer:
 - a combined product containing calcipotriol monohydrate and betamethasone dipropionate^[26] applied once daily for up to 4 weeks **or**
 - vitamin D or a vitamin D analogue^[27] applied once daily (only in those who cannot use steroids and with mild to moderate scalp psoriasis).
- 1.3.3.5 If continuous treatment with either a combined product containing calcipotriol monohydrate and betamethasone dipropionate^[26] applied once daily or vitamin D or a vitamin D analogue applied once daily for up to 8 weeks^[25] does

not result in clearance, near clearance or satisfactory control of scalp psoriasis offer:

- a very potent corticosteroid applied up to twice daily for 2 weeks for adults only or
- coal tar applied once or twice daily or
- referral to a specialist for additional support with topical applications and/or advice on other treatment options.
- 1.3.3.6 Consider topical vitamin D or a vitamin D analogue^{[27],[28]} alone for the treatment of scalp psoriasis only in people who:
 - are intolerant of or cannot use topical corticosteroids at this site or
 - have mild to moderate scalp psoriasis.
- 1.3.3.7 Do not offer coal tar-based shampoos alone for the treatment of severe scalp psoriasis.
- 1.3.4 Topical treatment of psoriasis affecting the face, flexures and genitals
- 1.3.4.1 Offer a short-term mild or moderate potency corticosteroid applied once or twice daily (for a maximum of 2 weeks because of the face, flexures or genitals.
- 1.3.4.2 Be aware that the face, flexures and genitals are particularly vulnerable to steroid atrophy and that corticosteroids should only be used for short-term treatment of psoriasis (1–2 weeks per month). Explain the risks to people undergoing this treatment (and their families or carers where appropriate) and how to minimise them.
- 1.3.4.3 For adults with psoriasis of the face, flexures or genitals if the response to short-term moderate potency corticosteroids is unsatisfactory, or they require continuous treatment to maintain control and there is serious risk of local corticosteroid-induced side effects, offer a calcineurin inhibitor^[30] applied twice daily for up to 4 weeks. Calcineurin inhibitors should be initiated by healthcare professionals with expertise in treating psoriasis.
- 1.3.4.4 Do not use potent or very potent corticosteroids on the face, flexures or

genitals.

- 1.3.4.5 When prescribing topical agents at facial, flexural and genital sites take into account that they may cause irritation and inform people undergoing treatment (and their families and carers where appropriate) of these risks and how to minimise them. See also recommendation 1.3.4.2.
- 1.4 Phototherapy (broad- or narrow-band UVB light and (PUVA)
- 1.4.1.1 Offer narrowband ultraviolet B (UVB) phototherapy to people with plaque or guttate-pattern psoriasis that cannot be controlled with topical treatments alone. Treatment with narrowband UVB phototherapy can be given 3 or 2 times a week depending on patient preference. Tell people receiving narrowband UVB that a response may be achieved more quickly with treatment 3 times a week.
- 1.4.1.2 Offer alternative second- or third-line treatment when:
 - narrowband UVB phototherapy results in an unsatisfactory response or is poorly tolerated **or**
 - there is a rapid relapse following completion of treatment (rapid relapse is defined as greater than 50% of baseline disease severity within 3 months) or
 - accessing treatment is difficult for logistical reasons (for example, travel, distance, time
 off work or immobility) or
 - the person is at especially high risk of skin cancer.
- 1.4.1.3 Consider psoralen[31] (oral or topical) with local ultraviolet A (PUVA) irradiation to treat palmoplantar pustulosis.
- 1.4.1.4 When considering PUVA for psoriasis (plaque type or localised palmoplantar pustulosis) discuss with the person:
 - other treatment options
 - that any exposure is associated with an increased risk of skin cancer (squamous cell carcinoma)
 - that subsequent use of ciclosporin may increase the risk of skin cancer, particularly if

- they have already received more than 150 PUVA treatments
- that risk of skin cancer is related to the number of PUVA treatments.
- 1.4.1.5 Do not routinely offer co-therapy with acitretin^[32] when administering PUVA.
- 1.4.1.6 Consider topical adjunctive therapy in people receiving phototherapy with broadband or narrowband UVB who:
 - have plaques at sites that are resistant or show an inadequate response (for example, the lower leg) to phototherapy alone, or at difficult-to-treat or high-need, covered sites (for example, flexures and the scalp), and/or
 - do not wish to take systemic drugs or in whom systemic drugs are contraindicated.
- 1.4.1.7 Do not routinely use phototherapy (narrowband UVB, broadband UVB or PUVA) as maintenance therapy.
- 1.4.1.8 Ensure that all phototherapy equipment is safety-checked and maintained in line with local and national policy^[33].
- 1.4.1.9 Healthcare professionals who are giving phototherapy should be trained and competent in its use and should ensure an appropriate clinical governance framework is in place to promote adherence to the indications for and contraindications to treatment, dosimetry and national policy on safety standards for phototherapy^[33].
- 1.4.2 Risk of skin cancer and how to minimise risk
- 1.4.2.1 Do not use PUVA in people with psoriasis of any type and a genetic predisposition to skin cancer for example, xeroderma pigmentosum or familial melanoma.
- 1.4.2.2 Do not use PUVA when other appropriate treatments are available in:
 - people with a personal history of skin cancer or
 - people who have already received 150 PUVA treatments or
 - children.

1.4.2.3 Use PUVA with caution or consider other treatment options in:

- people at risk of skin cancer (melanoma and non-melanoma type) (see 'Improving outcomes for people with skin tumours including melanoma' [NICE cancer service guidance])
- people with lighter skin types, such as skin types I or II on the Fitzpatrick scale [12]
- people who are likely to require ciclosporin or long-term methotrexate
- young people.
- 1.4.2.4 Offer lifetime skin cancer surveillance to people treated with PUVA who have:
 - had more than 150 PUVA treatments or
 - developed skin cancer.
- 1.4.2.5 Ensure that a permanent record of the person's cumulative number of UV treatments is kept (for example, in a national record).

1.5 Systemic therapy

1.5.1 General recommendations

- 1.5.1.1 Responsibility for use of systemic therapy should be in specialist settings only.

 Certain aspects of supervision and monitoring may be delegated to other healthcare professionals and completed in non-specialist settings, in which case, such arrangements should be formalised.
- 1.5.1.2 When offering systemic therapy, tailor the choice of agent and dosing schedule to the needs of the individual and include consideration of:
 - the person's age
 - disease phenotype, pattern of activity and previous treatment history
 - disease severity and impact
 - the presence of psoriatic arthritis (in consultation with a rheumatologist)
 - conception plans

- comorbidities
- the person's views.
- 1.5.1.3 Be aware of the benefits of, contraindications to and adverse effects associated with systemic treatments. Explain the risks and benefits to people undergoing this treatment (and their families or carers where appropriate), using absolute risks and natural frequencies when possible [9]. Support and advice should be provided by healthcare professionals who are trained and competent in the use of systemic therapies.
- 1.5.1.4 When reviewing response to systemic therapy, take into account:
 - disease severity compared with baseline (for example, <u>PASI</u> baseline to endpoint score)
 - control of psoriatic arthritis disease activity (in consultation with a rheumatologist if necessary)
 - the impact of the disease on the person's physical, psychological and social wellbeing
 - the benefits versus the risks of continued treatment
 - the views of the person undergoing treatment (and their family or carers where appropriate).
- 1.5.1.5 Monitor people using systemic treatment for all types of psoriasis in accordance with national and local drug guidelines and policy. Take appropriate action in the event of laboratory abnormalities or adverse events.
- 1.5.1.6 Offer adjunctive topical therapy to people with psoriasis using systemic therapy to optimise treatment outcomes.
- 1.5.1.7 Offer people with psoriasis who are starting treatment with a systemic non-biological or biological drug the opportunity to participate in long-term safety registries (for example the British Association of Dermatologists Biologic Interventions Register).
- 1.5.2 Systemic non-biological therapy
- 1.5.2.1 Offer systemic non-biological therapy to people with any type of psoriasis if:

- it cannot be controlled with topical therapy and
- it has a significant impact on physical, psychological or social wellbeing and
- one or more of the following apply:
 - psoriasis is extensive (for example, more than 10% of body surface area affected or a PASI score of more than 10) or
 - psoriasis is localised and associated with significant functional impairment and/ or high levels of distress (for example severe nail disease or involvement at highimpact sites) or
 - phototherapy has been ineffective, cannot be used or has resulted in rapid relapse (rapid relapse is defined as greater than 50% of baseline disease severity within 3 months).

Choice of drugs

- 1.5.2.2 Offer methotrexate^[34] as the first choice of systemic agent for people with psoriasis who fulfil the criteria for systemic therapy (see previous recommendation 1.5.2.1) except in the circumstances described in recommendations 1.5.2.4 and 1.5.2.12.
- 1.5.2.3 In people with both active psoriatic arthritis and any type of psoriasis that fulfils the criteria for systemic therapy (see recommendation 1.5.2.1) consider the choice of systemic agent in consultation with a rheumatologist.
- 1.5.2.4 Offer ciclosporin^[35] as the first choice of systemic agent for people who fulfil the criteria for systemic therapy (see recommendation 1.5.2.1) and who:
 - need rapid or short-term disease control (for example a psoriasis flare) or
 - have palmoplantar pustulosis or
 - are considering conception (both men and women) and systemic therapy cannot be avoided.
- 1.5.2.5 Consider changing from methotrexate to ciclosporin (or vice-versa) when response to the first-choice systemic treatment is inadequate.

- 1.5.2.6 Consider acitretin^[32] for adults, and in exceptional cases only for children and young people, in the following circumstances:
 - if methotrexate and ciclosporin are not appropriate or have failed or
 - for people with pustular forms of psoriasis.

Apremilast

See also NICE's technology appraisal guidance on <u>apremilast for treating moderate to severe</u> <u>plaque psoriasis</u> and <u>apremilast for treating active psoriatic arthritis</u>.

Drug regimens

- 1.5.2.7 Use incremental dosing of methotrexate (for example, starting with an initial dose of 5–10 mg once a week) and gradually increase up to an effective dose and a maximum of 25 mg a week. Assess the treatment response after 3 months at the target dose of methotrexate and stop treatment if the response is inadequate (for example, a decrease of less than 75% in <u>PASI</u> score or a decrease of less than 50% in <u>PASI</u> score and 5 points in <u>DLQI</u> score).
- 1.5.2.8 Use the lowest possible therapeutic dose of methotrexate to maintain remission.
- 1.5.2.9 Use 2.5–3 mg/kg a day of ciclosporin^[35]. Escalate to 5 mg/kg a day after 4 weeks only when there is no response to the lower dose or when rapid disease control is necessary (for example in severe unstable disease). Assess the treatment response after 3 months at the optimum dose of ciclosporin and stop treatment if the response is inadequate (for example, less than a 75% decrease in PASI score or less than a 50% decrease in PASI score and less than 5 points in DLQI score).
- 1.5.2.10 Use the lowest possible therapeutic dose of ciclosporin to maintain remission for up to 1 year. Consider other treatment options when disease relapses rapidly on stopping ciclosporin therapy (rapid relapse is defined as greater than 50% of baseline disease severity within 3 months of stopping treatment). Do not use ciclosporin continuously for more than 1 year unless disease is severe or unstable and other treatment options, including systemic biological therapy, cannot be used.

- 1.5.2.11 Use incremental dosing of acitretin^[32] to minimise mucocutaneous side effects and achieve a target dose of 25 mg daily in adults. Consider dose escalation to a maximum of 50 mg daily when no other treatment options are available. Assess the treatment response after 4 months at the optimum dose of acitretin and stop treatment if the response is inadequate, for example:
 - in plaque-type psoriasis, less than a 75% decrease in <u>PASI</u> score or less than a 50% decrease in <u>PASI</u> score and less than 5 points in <u>DLQI</u> score
 - in pustular forms of psoriasis, not achieving clear or nearly clear on the static Physician's Global Assessment.

Methotrexate and risk of hepatotoxicity

1.5.2.12 When considering the risks and benefits of treating any type of psoriasis with methotrexate, be aware that methotrexate can cause a clinically significant rise in transaminases and that long-term therapy may be associated with liver fibrosis (see recommendations 1.5.2.13 to 1.5.2.16).

Methotrexate and monitoring for hepatotoxicity

- 1.5.2.13 Before and during methotrexate treatment, offer the person with any type of psoriasis an evaluation for potential risk of hepatotoxicity. Use standard liver function tests and serial serum procollagen III levels to monitor for abnormalities during treatment with methotrexate, taking into account preexisting risk factors (for example obesity, diabetes and alcohol use), baseline results and trends over time.
- 1.5.2.14 When using serum procollagen III levels to exclude liver fibrosis or cirrhosis, be aware that the:
 - test cannot be used in children and young people
 - results may be unreliable in people with psoriatic arthritis
 - estimated positive predictive value is 23–95% and the estimated negative predictive value is 89–100%.
- 1.5.2.15 Provide advice on modifiable risk factors for liver disease prior to and during therapy, including alcohol intake and weight reduction if appropriate in line with

the NICE guidelines on <u>alcohol-use disorders</u>: <u>prevention</u> and <u>obesity</u> <u>prevention</u>. For further advice on how to support attitude and behavioural change see the NICE guideline on <u>behaviour change</u>.

1.5.2.16 Seek timely specialist advice and consider referral to a clinician with expertise in liver disease if the results of liver tests are abnormal.

1.5.3 Systemic biological therapy

The GDG did not review evidence for any aspect of the use of a first biological agent because guidance on this is already available in the existing NICE technology appraisals^[36].

- 1.5.3.1 Biological agents for psoriasis should be initiated and supervised only by specialist physicians experienced in the diagnosis and treatment of psoriasis.
- 1.5.3.2 If a person has both psoriasis and psoriatic arthritis, take into account both conditions before initiating or making changes to biological therapy and manage their treatment in consultation with a rheumatologist (see also the NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis [137], ustekinumab for treating active psoriatic arthritis after inadequate response to DMARDs [137] and golimumab for the treatment of psoriatic arthritis [137], and the NICE guideline on spondyloarthritis in over 16s).
- 1.5.3.3 When using the <u>DLQI</u>, healthcare professionals should take into account any physical, sensory or learning disabilities, or communication difficulties that could affect the responses to the DLQI and make any adjustments they consider appropriate.

Adalimumab in adults

For guidance on treating psoriasis with adalimumab^[37] see NICE's technology appraisal on adalimumab for the treatment of adults with psoriasis.

Etanercept in adults

For guidance on treating psoriasis with etanercept^[37] see NICE's technology appraisal on <u>etanercept</u> and <u>efalizumab</u> for the treatment of adults with psoriasis.

Infliximab in adults

For guidance on treating psoriasis with infliximab $^{[37]}$ see NICE's technology appraisal on infliximab for the treatment of adults with psoriasis.

Ixekizumab in adults

For guidance on treating psoriasis with ixekizumab see NICE's technology appraisal on <u>ixekizumab</u> <u>for treating moderate to severe plaque psoriasis</u>.

Secukinumab in adults

For guidance on treating psoriasis with secukinumab see NICE's technology appraisal on secukinumab for treating moderate to severe plaque psoriasis.

Ustekinumab in adults

For guidance on treating psoriasis with ustekinumab^[38] see NICE's technology appraisal on ustekinumab for the treatment of adults with moderate to severe psoriasis.

Adalimumab, etanercept and ustekinumab in children and young people

For guidance on treating psoriasis with adalimumab^[37], etanercept^[37] and ustekinumab^[38] see NICE's technology appraisal on adalimumab, etanercept and ustekinumab for treating plaque psoriasis in children and young people.

Changing to an alternative biological drug

- 1.5.3.4 Consider changing to an alternative biological drug in adults if:
 - the psoriasis does not respond adequately to a first biological drug as defined in NICE technology appraisals^[39] (at 10 weeks after starting treatment for infliximab, 12 weeks for etanercept, ixekizumab and secukinumab, and 16 weeks for adalimumab and ustekinumab; primary failure) or
 - the psoriasis initially responds adequately but subsequently loses this response, (secondary failure) or
 - the first biological drug cannot be tolerated or becomes contraindicated.
- 1.5.3.5 For adults in whom there is an inadequate response to a second biological drug,

seek supra-specialist advice from a clinician with expertise in biological therapy.

More information

You can also see this guideline in the NICE Pathway on psoriasis.

To find out what NICE has said on topics related to this guideline, see our web page on skin conditions.

See also the guideline committee's discussion and the evidence reviews (in the <u>full guideline</u>), and information about <u>how the guideline was developed</u>, including details of the committee.

^[9]See the <u>appendix</u> for details of the risk-benefit profiles of interventions recommended in this guideline.

^[10]See Feldman SR, Krueger GG (2005) Psoriasis assessment tools in clinical trials. Annals of Rheumatic Disease 64 (Suppl. 2): ii65–ii68.

See <u>Psoriasis Area and Severity Index</u>. The PASI is also available from the <u>British Association of Dermatologists</u> website.

Fitzpatrick scale: type I: always burns, never tans; type II: usually burns, tans with difficulty, type III: sometimes mild burn, gradually tans; type IV: rarely burns, tans with ease; type V: very rarely burns, tans very easily; type VI: never burns, tans very easily.

See Rich P, Scher RK (2003) Nail Psoriasis Severity Index: a useful tool for evaluation of nail psoriasis. Journal of the American Academy of Dermatology 49: 206–12.

^[14] See <u>Dermatology Life Quality Index</u>. The DLQI is also available from the <u>British Association of</u> <u>Dermatologists</u> website.

^[15] See also recommendation 1.5.3.3.

^[16] See Children's Dermatology Life Quality Index.

See: Ibrahim GH, Buch MH, Lawson C et al. (2009) Evaluation of an existing screening tool for psoriatic arthritis in people with psoriasis and the development of a new instrument: the Psoriasis Epidemiology Screening Tool (PEST) questionnaire. Clinical and Experimental Rheumatology 27: 469–74. The PEST questionnaire is reproduced in appendix T of the <u>full guideline</u>.

- Severe psoriasis was defined as either requiring treatment with phototherapy or systemic agents or requiring hospital admission in the studies underpinning this recommendation.
- [19] Severe psoriasis was identified by hospitalisations (including outpatient visits) for psoriasis (ICD-10 L40) or psoriatic arthritis.
- [20] See recommendations 1.3.4.2 and 1.3.4.4 for details on safe use of steroids at facial, flexural and genital sites.
- [21] See recommendations 1.3.1.12 and 1.3.1.13 for details on safe duration of steroid use.
- See recommendation 1.3.1.8 for additional considerations before changing to the next treatment option.
- As of August 2017, there are currently different topical calcipotriol preparations available in the UK which vary in their licensing status for use in children and young people under 18. Additionally, potent topical corticosteroid preparations available in the UK vary in the age from which they are licensed for use in children. Please refer to the BNF for children for general information on appropriate dosing and duration of treatment with these preparations. Refer to the Summary of Product Characteristics for specific information on individual topical calcipotriol and corticosteroid preparations.
- As of August 2017, there are several potent topical corticosteroid preparations available in the UK, and the age from which they are licensed for use in children varies. Refer to the Summary of Product Characteristics for information on individual potent topical corticosteroid preparations.
- ^[25] In children and young people the specified duration of therapy may not be appropriate. Please refer to the BNF for children for information on appropriate dosing and duration of treatment.
- At the time of publication (October 2012), the combined product containing calcipotriol monohydrate and betamethasone dipropionate did not have UK marketing authorisation for this indication in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's <u>Good practice in prescribing medicines guidance for doctors</u> for further information.
- ^[27] As of August 2017, topical calcitriol and tacalcitol preparations available in the UK were not licensed for use in children. Topical calcipotriol preparations available in the UK vary in their

licensing status for use in children and young people under 18. Refer to the Summary of Product Characteristics for specific information on individual topical calcipotriol preparations.

Please refer to the BNF for children for information on appropriate dosing and duration of treatment.

At the time of publication (October 2012), moderate potency corticosteroids did not have UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's <u>Good practice in prescribing medicines – guidance for doctors</u> for further information.

At the time of publication (October 2012), topical calcineurin inhibitors did not have UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's <u>Good practice in prescribing medicines – guidance for doctors</u> for further information.

At the time of publication (October 2012), psoralen did not have UK marketing authorisation for this or any indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the GMC's <u>Good practice in prescribing medicines – guidance for doctors</u> for further information.

See the Medicines and Healthcare products Regulatory Agency guidance on <u>Oral retinoid</u> medicines: revised and simplified pregnancy prevention educational materials for healthcare professionals and women (June 2019). See also the Summary of Product Characteristics for further information on this issue.

See: <u>British Association of Dermatologists standards for phototherapy</u> and <u>Guidelines on the</u> measurement of ultraviolet radiation levels in ultraviolet phototherapy.

At the time of publication (October 2012), methotrexate did not have UK marketing authorisation for this indication in children and young people. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's <u>Good practice in prescribing medicines – guidance for doctors</u> for further information.

At the time of publication (October 2012), ciclosporin did not have UK marketing authorisation for this indication in children and young people under 16 years of age. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's <u>Good practice in prescribing medicines – guidance for doctors</u> for further information.

NICE technology appraisal guidance $\underline{103}, \underline{134}, \underline{146}, \underline{180}, \underline{350}, \underline{442}$ and $\underline{455}$.

See the Medicines and Healthcare products Regulatory Agency Drug Safety Update on <u>Tumour</u> necrosis factor alpha inhibitors – risk of tuberculosis (April 2014).

See the Medicines and Healthcare products Regulatory Agency Drug Safety Update on <u>Ustekinumab (Stelara): risk of exfoliative dermatitis</u> (January 2015).

[39] See NICE technology appraisal guidance <u>103</u>, <u>134</u>, <u>146</u>, <u>180</u>, <u>350</u> and <u>442</u>.

2 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the <u>full guideline</u>.

2.1 Assessment of disease severity and impact

In children, young people and adults with psoriasis, can tools be developed and/or existing ones further refined and validated to:

- assess disease severity and impact in both non-specialist and specialist healthcare settings, to facilitate assessment, appropriate referral, treatment planning and measurement of outcomes
- measure burden and cumulative effect of disease activity, severity and impact for people with both psoriasis and psoriatic arthritis?

Why this is important

Assessment of disease severity and impact is fundamental to delivering high-quality health care and measuring outcomes. The evidence review indicates that the existing tools have important limitations, and have not been validated in relevant healthcare settings or in children or young people. Future research should ensure that tools are developed that capture information on site of involvement as well as extent and the impact of previous treatments. Tools should capture all aspects of impact on life including physical, psychological and social wellbeing and factors that may influence this impact, such as distress and beliefs about psoriasis. Tools that can be used by patients (as well as healthcare professionals) to assess disease severity and that encompass new technologies should be evaluated to facilitate, when appropriate, modern healthcare delivery models (for example, remote monitoring of disease activity).

In addition, understanding the true burden and effect of disease activity, severity and impact for both psoriasis and psoriatic arthritis has not previously been comprehensively studied. Capturing this information and distilling out significant factors for focused investigation will lead to better understanding of the needs of this particular group of people and the impact of treatments that benefit both disease compartments (skin and joints).

2.2 Methotrexate and risk of hepatotoxicity

What is the impact of methotrexate compared with other approaches to care (for example other

systemic non-biological or biological treatments) on risk of significant liver disease in people with psoriasis and do risk factors such as obesity, alcohol use or diabetes alter this risk?

Why this is important

The evidence review indicates that people with psoriasis may be at risk of liver disease, and there is great uncertainty about the contributing role of methotrexate. Clinician and patient concerns about this side effect are a common cause of treatment discontinuation. However, existing studies are poorly controlled for important confounders and many are very old. Methotrexate is a low cost intervention that is effective in an important proportion of patients. Research in this area will properly delineate the size of risk and how to minimise it. Future research should be adequately powered to detect clinically relevant liver disease, use relevant tools to do so, and properly control for relevant confounders.

2.3 Rapid escalation to systemic treatments

In people with psoriasis, does early intervention with systemic treatments improve the long-term prognosis of psoriasis severity, comorbidities (including psoriatic arthritis), or treatment-related adverse effects, and are there any clinical (for example demographic or phenotypic) or laboratory (for example genetic or immune) biomarkers that can be used to identify those most likely to benefit from this treatment approach?

Why this is important

At present the treatment pathway for people with psoriasis follows clinical need as no studies have been conducted to evaluate whether early intervention with systemic treatments alters prognosis. Consequently, patients with more severe disease sequence through all therapies in the treatment pathway, with a proportion requiring high-cost biological interventions to maintain disease control. The evidence indicates that there are very few treatment options for people with chronic disease, all of them are associated with side effects, many are co-dependent (for example escalated risk of skin cancer in people treated with the phototherapy and ciclosporin sequence), and loss of response to biological therapies is a significant clinical issue. If early intervention with systemic treatments was shown to alter the prognosis, particularly if there were markers that could stratify those likely to benefit, this would be of major importance to patients, and likely to deliver much more cost-effective treatment strategies.

2.4 Self-management

Do structured psoriasis-focused self-management programmes improve patient confidence,

wellbeing and disease control compared with standard care?

Why this is important

Virtually all patients self-manage their condition to a greater or lesser extent and this involves complex topical applications as well as systemic therapies to be used over many years in response to fluctuating disease severity. The evidence indicates that in contrast to many chronic disorders, there are no validated programmes to help patients achieve effective self-management. Establishing a focused programme that effectively improves outcomes for patients would be of clinical benefit and likely deliver healthcare savings.

2.5 Topical therapy

In people of all ages with psoriasis:

- 1. How should topical therapies be used to maintain disease control i) safely; ii) effectively and iii) what are the health economic implications?
- 2. What are the risks of 'real life' long term corticosteroid use, are there particular people at risk and what strategies can be used to modify or avoid risks?

Why this is important

Currently, topical therapies, in some form or another, are prescribed to virtually everyone with psoriasis, often as first line psoriasis treatment and they are also frequently used adjunctively with other interventions. There is a wide array of potential topical agents available and further research specifically targeting therapeutic strategies together with sequencing of topical agents for maintaining disease control in the long term continues to deserve focused attention. In addition exploration of the risks associated with long term corticosteroid use and strategies aimed at modifying risk would be a critical element of this research to fill the current gap in the literature.

Update information

September 2017: We revised the guideline throughout to link to other NICE guidance (including technology appraisals) and some relevant non-NICE guidelines, as well as including new MHRA safety advice and updated licensing information.

Minor updates since publication

August 2019: Links to the MHRA safety advice on the risk of using retinoids in pregnancy have been updated to the June 2019 version. Links also updated throughout to the Dermatology Life Quality Index pages at Cardiff University's website.

Appendix: Information to facilitate discussion of risks and benefits of treatments for people with psoriasis

Data are provided for the proportions of people achieving remission, withdrawing due to adverse events and experiencing specific adverse events (as prioritised by the GDG) for interventions that have been recommended in this guideline. Data are based on pooled estimates where possible and from trials with populations and dosing appropriate to the intervention. For full details of the duration of treatment and dosing schedules please refer to the main text of the guideline.

Text is labelled with an asterisk when the GDG had very low confidence in the absolute estimates, for example due to confounding and inadequate sample size.

For a landscape version of the following table, please refer to the <u>full version of the guideline</u>.

Topical therapies (short-term)

Population (psoriasis phenotype)	N achieving remissions (clear/nearly clear or PASI75)	N experiencing:		
		Withdrawal due to drug toxicity	Serious/ named adverse events	
Vitamin D or vitamin D analogues				
Chronic plaque	Intervention	Intervention	Intervention	
psoriasis of trunk and limbs	Once daily: 220/1000 Twice daily: 487/1000	Once or twice daily: 23/1000	Skin atrophy Twice daily: 1.9/1000	
	Placebo	Placebo	Placebo	
	Once daily: 76/1000 Twice daily: 122/1000	Once or twice daily: 29/1000	Skin atrophy Twice daily: 3.2/1000	
	No active comparator ¹			

Children with Interven		ntion	Intervent	ion	Intervention
chronic plaque psoriasis of trunk and limbs*	Twice daily: 605/1000*		NA*		NA*
	Placebo)	Placebo		Placebo
	Twice d	aily: 441/1000*	NA*		NA*
	No activ	ve comparator ¹			NA*
Scalp psoriasis	Interve	ntion	Intervent	ion	Intervention
	Once da	aily: 387/1000	Once dail	y: 81/1000	NA
	Placebo)	Placebo		Placebo
	Once da	aily: 219/1000	Once dail	y: 52/1000	NA
	No activ	ve comparator ¹			
Potent corticoster	oids				
Chronic plaque pso	oriasis	Intervention		Intervention	Intervention
of trunk and limbs	of trunk and limbs		aily: 394/	Once daily: 10/1000 Twice daily: 25/1000	Skin atrophy Once or twice daily: 5.5/1000
		Placebo		Placebo	Placebo
		Once or twice da	aily: 77/	Once daily: 79/1000 Twice daily: 0/1000	Skin atrophy Once or twice daily: 0/1000
		No active compa	rator ¹		
Scalp psoriasis		Intervention		Intervention	Intervention
		Once or twice da	aily: 632/	Once or twice daily: 9.5/1000	NA
		Placebo		Placebo	Placebo
		Once or twice daily: 223/ 1000		Once or twice daily: 41/1000	NA

	No active comparator ¹		NA	
Vitamin D or analogue and	potent steroid, applied one	in the morning and one ir	the evening	
Chronic plaque psoriasis	Intervention	Intervention	Intervention	
of trunk and limbs	611/1000	13/1000	NA	
	No placebo			
	Active comparator	Active comparator	Active comparator	
	Calcipotriol Twice daily 469/1000	Calcipotriol Twice daily 26/1000	NA	
Combined vitamin D or an	alogue and potent steroid			
Chronic plaque psoriasis	Intervention	Intervention	Intervention	
of trunk and limbs	Once daily: 494/1000	Once daily: 7.5/1000	Skin atrophy	
			Once daily: 4.2/1000	
	No placebo			
	Active comparator	Active comparator	Active comparator	
	Vitamin D Once daily: 193/1000	Vitamin D Once or twice daily: 27/1000	Skin atrophy Vitamin D Twice daily: 1.8/1000	
Scalp psoriasis	Intervention	Intervention	Intervention	
	Once daily: 800/1000	Once daily: 17/1000*	NA	
	Placebo	Placebo	Placebo	
	Once daily: 500/1000	Once daily: 0/1000*	NA	
	No active comparator ¹			
Very potent corticosteroic	ls			
Chronic plaque psoriasis of trunk and limbs	Intervention	Intervention	Intervention	

	Once or twice daily: 625/ 1000	Once or twice daily: 4.6/1000	Skin atrophy Once or twice daily: 23/1000
	Placebo	Placebo	Placebo
	Once or twice daily: 13/ 1000	Once or twice daily: 6.0/1000	Skin atrophy Once or twice daily: 0/1000
	No active comparator ¹		
Scalp psoriasis	Intervention	Intervention	Intervention
	Once or twice daily: 646/ 1000	Once or twice daily: 0/ 1000	Skin atrophy Once or twice daily: 0/1000
	Placebo	Placebo	Placebo
	Once or twice daily: 80/ 1000	Placebo Once or twice daily: 5.9/1000	Placebo Skin atrophy Once or twice daily: 11/1000
	No active comparator ¹		
Tazarotene			
Chronic plaque psoriasis	Intervention	Intervention	Intervention
of trunk and limbs	Once daily: 58/1000	Once daily: 107/1000	Skin atrophy Once daily: 0/1000
	Placebo	Placebo	Placebo

	Once daily: 20/1000	Once daily: 44/1000	Skin atrophy Once daily:	
			0/1000	
	No active comparator ¹			
Short-contact dithranol ²				
Chronic plaque psoriasis	Intervention	Intervention	Intervention	
of trunk and limbs	Once daily: 430/1000	Once daily: 82/1000	NA	
	No placebo			
	Active comparator	Active comparator	Active comparator	
	Calcipotriol twice daily: 588/1000	Calcipotriol twice daily: 39/1000	NA	
Coal tar				
Chronic plaque psoriasis	Intervention	Intervention	Intervention	
of trunk and limbs*	Once or twice daily: 111/ 1000 to 519/1000 depending on formulation and follow-up*	Once or twice daily: 0–56/1000 depending on formulation and follow-up*	NA*	
	No placebo			
	Active comparator	Active comparator	Active comparator	
	Calcipotriol Twice daily: 214/1000 to 723/1000 depending on follow-up*	Calcipotriol Twice daily: 0-40/1000 depending on follow- up*	NA*	
Tacromilus				
Psoriasis of the face and	Intervention	Intervention	Intervention	
flexures*	Twice daily: 652/1000*	Twice daily: 0/1000*	NA*	
	Placebo	Placebo	Placebo	

	Twice daily: 309/1000*	Twice daily: 25/1000*	NA*			
	No active comparator ¹					
Pimecrolimus						
Psoriasis of the flexures*	Intervention	Intervention	Intervention			
	Twice daily: 714/1000*	Twice daily: 0/1000*	Skin atrophy Twice daily: 0/1000*			
	Placebo	Placebo	Placebo			
	Twice daily: 207/1000*	Twice daily: 0/1000*	Skin atrophy Twice daily: 0/1000*			
	No active comparator ¹					

Abbreviations: NA, not available.

Phototherapy (short-term)

Population (psoriasis phenotype)	N achieving remissions (clear/ nearly clear or PASI75)	N experiencing:	
		Withdrawal due to drug toxicity	Serious/named adverse events
NBUVB vs PUV	Ą		
Plaque	Intervention	Intervention	Intervention
psoriasis	Twice weekly 647/1000	Twice weekly 38/1000	NA

^{*} GDG had very low confidence in the absolute estimates, for example due to confounding and inadequate sample size.

¹ An active comparator will only be included if no placebo comparison is available; the standard intervention will be chosen if multiple active comparators are available.

 $^{^{2}}$ 2/3 studies reported home-use of dithranol and in 1/3 studies the setting was unclear.

	No placebo	No placebo				
	Active com	parator	Active comparator	Active comparator		
	Oral PUVA 915/1000	(twice weekly)	Oral PUVA (twice weekly) 47/1000	NA		
PUVA (oral)						
Palmoplantar	Intervention	on	Intervention	Intervention		
pustulosis	3-4 times v 941/1000	weekly	3-4 times weekly 29/1000*	Burn 3-4 times weekly 147/1000*		
	Placebo		Placebo	Placebo		
	No treatme 500/1000	ent	No treatment 0/1000*	No treatment 0/1000*		
	No active o	omparator ¹				
PUVA (cream)	'					
Palmoplantar p	oustulosis*	Intervention	Intervention	Intervention		
		3 times weekly 952/1000*	3 times weekly 45/1000*	NA*		
		No placebo				
		Active comparator	Active comparator	Active comparator		
		NBUVB 3 times weekly 429/1000*	NBUVB 3 times weekly 0/1000*	NA*		
NBUVB plus vi	tamin D or an	alogues	1			
Plaque psorias	is*	Intervention	Intervention	Intervention		

		3 times weekly UV + Twice daily topical 900/1000*	3 times weekly UV + Twice daily topical 50/1000*	Burn 3 times weekly UV + Twice daily topical 200/1000*
		No placebo Active comparator	Active comparator*	Active comparator*
DDI IV/D l i'd	one in Danamak	3 times weekly NBUVB alone 611/1000*	3 times weekly NBUVB alone 28/1000*	Burn 3 times weekly NBUVB alone 111/1000*
BBUVB plus vit	Intervention	ogues 	Intervention	Intervention
psoriasis*		weekly UV + Twice		NA*
	No placebo*		1	I
	Active compa	arator	Active comparator	Active comparator
	BBUVB alone weekly 208/1000*	e up to 3 times	BBUVB alone up to 3 times weekly 19/1000*	NA*
Liquor carbonio	distillate (equi	valent 2.3% coal tar)	plus NBUVB	
Plaque	Intervention		Intervention	Intervention
psoriasis*	Clear (3 time daily topical) 583/1000*	s weekly UV+ twice	3 times weekly UV + twice daily topical 0/1000*	Burn 3 times weekly UV + twice daily topical 167/1000*

	No placebo			
	Active comparator		Active comparator	Active comparator
	3 times week	dy	3 times weekly	Burn
	NBUVB alon	е	NBUVB alone	NBUVB alone 3
	500/1000*		0/1000*	times weekly
				167/1000*
Dithranol plus B	BUVB			
Psoriasis*		Intervention	Intervention	Intervention
		3 times weekly UV + twice daily topical 625/1000*	NA*	NA*
		No placebo		
		Active comparator	Active comparator	Active comparator
		3 times weekly BBUVB alone 458/1000*	NA*	NA*

Abbreviations: BBUVB, broadband UVB; NA, not available, NBUVB, narrowband UVB; PUVA, psoralen plus UVA.

Systemic, non-biologic therapies (short-term)

Population (psoriasis phenotype)	N achieving remissions (clear/nearly clear or PASI75)	N experiencing:	
		Withdrawal due to drug toxicity	Serious/named adverse events

^{*} The GDG had very low confidence in the absolute estimates, for example due to confounding and inadequate sample size.

¹ An active comparator will only be included if no placebo comparison is available; the standard intervention will be chosen if multiple active comparators are available.

Methotrexate; incremen	Methotrexate; incremental dosing (plus folic acid)				
Chronic plaque psoriasis	Intervention	Intervention	Intervention		
	415/1000	55/1000*	Elevated liver enzymes (>1.5-2.5 ULN) 91/1000*		
	Placebo	Placebo	Placebo		
	188/1000	20/1000*	Elevated liver enzymes (>1.5-2.5 ULN) 75/1000*		
Ciclosporin					
Chronic plaque	Intervention	Intervention	Intervention		
psoriasis	2.5-3 mg 232/1000 5 mg 600/1000	0/1000*	Hypertension 391/1000 Decrease in GFR >15% 3 mg/kg: 333/1000 5 mg/kg: 500/1000*		
	Placebo	Placebo	Placebo		
	44/1000	0/1000*	Hypertension 333/1000 Decrease in GFR >15% 0/1000*		
Ciclosporin					
Palmoplantar pustulosis	Intervention	Intervention	Intervention		
	652/1000	NA	Hypertension 37/1000*		
	Placebo	Placebo	Placebo		

	200/1000	NA	Hypertension 0/1000*			
Acitretin – 25 mg						
Plaque, pustular and	Intervention	Intervention	Intervention			
erythrodermic psoriasis*	480/1000*	18/1000*	Cheilitis			
ps01 18515			850/1000			
			Hair loss			
			150/1000			
			Elevated liver			
			enzymes (>ULN)			
			200/1000			
			Elevated cholesterol (>ULN)			
			0/1000*			
	DI I	DI I				
	Placebo	Placebo	Placebo			
	188/1000* 0/1000*		Cheilitis			
			300/1000			
			Hair loss			
			100/1000			
			Elevated liver			
			enzymes (>ULN)			
			0/1000			
			Elevated cholesterol (>ULN)			
			53/1000*			

Abbreviations: GFR, glomerular filtration rate; NA, not available; ULN, upper limit of normal.

^{*} The GDG had very low confidence in the absolute estimates, for example due to confounding and inadequate sample size.

Systemic, biologic therapies (short-term)

Population (psoriasis phenotype)	Prior biologics received	N achieving remissions (clear/nearly clear or PASI75)	N experiencing withdrawal due to drug toxicity or serious adverse events		
Infliximab					
Adults with	Unclear	Intervention	Intervention		
severe plaque psoriasis and		723/1000	NA		
prior biologic		Placebo	Placebo		
exposure		0/1000*	NA		
		No active comparator ¹			
Etanercept					
Adults with	Included etanercept, infliximab, and adalimumab (proportions unclear)*	Intervention	Intervention		
severe plaque psoriasis and		370/1000*	NA*		
prior biologic		Placebo	Placebo		
exposure*		NA*	NA*		
		Active comparator	Active comparator		
		Ustekinumab 556/1000*	NA*		
Ustekinumab					
Adults with	Included etanercept, infliximab,	Intervention	Intervention		
severe plaque psoriasis and	and adalimumab (proportions unclear)	619/1000	NA		
prior biologic		Placebo	Placebo		
exposure		170/1000	NA		
		No active comparator ¹			

Adalimumab					
Adults with severe plaque psoriasis*	plaque (23.1%), ustekinumab (23.1%),		Intervention NA* Placebo		
	(20.5%), and other (17.7%)	Placebo NA* Active	NA* Active comparator		
	comparator No prior biologic	NA*			
		744/1000*			

Abbreviations: NA, not available.

Long-term risks

Outcome(s)	Population – psoriasis phenotype	Number experiencing event
PUVA (oral)		

^{*} The GDG had very low confidence in the absolute estimates, for example due to confounding and inadequate sample size.

¹ An active comparator will only be included if no placebo comparison is available; the standard intervention will be chosen if multiple active comparators are available.

Skin cancer – SCC	Plaque (84%), guttate (12%) and erythrodermic (4%)	Relative risk compared with the general population				
	psoriasis		PUVA exposures		RR	
			<100		5.1	(3.5-7.2)
			100-159		8.4 (5.6	5-12.1)
			160-336 ≥337		26.5 (22.2-31.4)	
					68.5 (54.9-84.5)	
		Absolute increase		se ir	n risk	
			PUVA exposures	SC	Cs	% increase in 10-year risk
			<100	18	3	1.7%
			100-159	15	5	2.7%
			160-336	68	3	8.8%
			≥337	34		12.7%
NBUVB						
Skin cancer	Insufficient data available					
Methotrexate						
Liver fibrosis, bone marrow suppression and pneumonitis	No long-term data available					
Ciclosporin						

Hypertension, renal impairment, gout and hyperuricaemia	No long-term data available	
Acitretin		
Hyperlipidaemia, hepatotoxicity, skeletal AEs and cheilitis	No long-term data available AEs	
Abbreviations: PUVA, psoralen plus UVA; RR, relative risk; SCC, squamous cell carcinoma.		

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Accreditation

